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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/619,032	07/19/2000	Dennis Murphy	DIVER1120-3	2212

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/02/2002 16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/619,032	MURPHY ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-12 are pending.

It is noted that the examination of the instant application has been assigned to a different Examiner in Group Art Unit 1652.

Applicant's amendment of claims 7 and 9 in Paper No. 9, filed on 3/6/2002 is acknowledged.

Applicant's submission of a new sequence listing in paper and computer-readable form in Paper No. 14, filed on 9/20/2002 is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

1. The specification is objected to for not complying with sequence rules. The newly submitted Sequence Listing (paper and CRF) contains a sequence which is not supported by the specification as originally filed. See 37 CFR 1.825(a).

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 10/18/2002 was filed after the mailing date of the first Office Action on 9/28/2001. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Priority

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 09/407806, filed on 9/28/1999, and 08/613220, filed on 3/8/1996.

4. It is noted that while the polypeptide of SEQ ID NO: 4 in US application No. 08/613220 is disclosed in Figure 1 as having 364 amino acids, it is disclosed in its CRF as not being the same as the polypeptide of SEQ ID NO: 4 (346 amino acids instead) of the instant application. Therefore, the priority date applied to the polypeptide of SEQ ID NO: 4 is 9/28/1999.

Drawings

5. The drawings as originally filed have been reviewed and are approved by a draftsperson under 37 CFR 1.84 or 1.152. It is noted, however, that Figure 1 no longer depicts the nucleotide and amino acid sequences of SEQ ID NO: 3 and 4 as amended.

Claim Rejections - 35 USC § 112, Second Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 1 and 6 (claims 2-5, 7-12 dependent thereon) are indefinite in the recitation of "α-galactose bond" as it is unclear what the meaning of the term is and the specification does not provide a clear definition of the term. As known in the art, α-galactose is a simple sugar

(monosaccharide). Therefore, one of skill in the art cannot discern if the term refers to (1) bonds within the α-galactose structure (i.e. carbon-carbon, hydrogen-oxygen, carbon-hydrogen, or carbon-oxygen bonds), (2) bonds linking one α-galactose sugar with another α-galactose or (3) bonds linking one α-galactose sugar with a different sugar. For examination purposes, the term will be interpreted as "any bond". Correction is required.

9. This rejection was previously applied to claims 1, 6 and 7 in Paper No. 6, mailed on 9/28/2001.

10. Applicants argue that one of skill in the art would know that the term "α-galactose bond" refers to a bond of an α-galactose residue that is hydrolyzed by α-galactosidase and that the term itself indicates that it is a bond of a galactose residue. In addition, Applicants argue that the claim indicates that an "α-galactose bond" is a bond which is hydrolyzed by the enzyme of SEQ ID NO: 4.

11. Applicants arguments have been fully considered but are not deemed persuasive to overcome the rejection. As explained in the rejection above, the term can have different interpretations. Furthermore, it appears that Applicant's own definition of the term "α-galactose bond" as argued above is contradictory. One would interpret Applicant's argument of "bond of an α-galactose residue that is hydrolyzed by the enzyme" as meaning "bond between an α-galactose residue and another sugar residue", while the following argument "bond of a galactose residue" would be interpreted as "any bond within the structure of the α-galactose residue. Since it is well known in the art that α-galactosidases hydrolyze α-1,6-linked α-galactose residues, it is suggested that the term be amended to recite "α-1,6 galactosyl bond or α-1,6 galactosidic bond" if the intended bond is that between two monosaccharides.

12. Claim 9 is indefinite in the recitation of "a combination of a compound of a member of the lentil family and a compound of a member of the bean family" as it is unclear what the meaning of the term is within the context of the claim. As written, the claim is directed to one compound (i.e. a polysaccharide), however since the term recites "combination" one cannot establish if the compound can also be a mixture of polysaccharides from lentils and beans, or a hybrid polysaccharide formed from a saccharide from lentils and a saccharide from beans. It is suggested that the "combination" be clearly defined. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-2, 5-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-2, 5-12 are directed to a method for hydrolyzing a genus of bonds with a genus of enzymes having at least 70% amino acid sequence identity to the polypeptide of SEQ ID NO: 4. While the specification discloses the structure and function of the polypeptide of SEQ ID NO: 4, there is no disclosure of the function of other enzymes having at least 70% sequence identity to that of SEQ ID NO: 4. In addition, while it is known in the art which type of bonds are hydrolyzed by α-galactosidases (see discussion above, rejections under 35 USC 112, second

paragraph), there is no disclosure of which bonds are hydrolyzed by enzymes of any function having 70% sequence identity to SEQ ID NO: 4. There is no disclosure of the critical structural elements an enzyme having 70% sequence identity to SEQ ID NO: 4 should have to hydrolyze the recited bonds (see interpretation above, rejections under 35 USC 112, second paragraph) or to hydrolyze α-1,6 galactosyl bonds (i.e. α-galactosidase activity).

While one can argue that function can be inferred by sequence comparison with a known protein of known function, the state of the art teaches that sequence comparison alone should not be used to determine a protein's function and that small amino acid changes can drastically change the function of a polypeptide. Bork (Genome Research, 10:348-400, 2000) teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where found to be hydroxylases once tested for activity. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Many functionally unrelated polypeptides with enzymatic activity are encompassed within the scope of these claims. The specification only discloses a single species of the claimed genus required to practice the claimed method which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of the claimed method. Thus, one skilled in the art

cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

15. Claims 1-2, 5-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for hydrolyzing α-1,6 galactosyl bonds with the α-galactosidase of SEQ ID NO: 4, does not reasonably provide enablement for a method for hydrolyzing any bond with any enzyme which is at least 70% sequence identical to SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims is not commensurate with the enablement provided in regard to the large number of unknown enzymes and bonds hydrolyzed by those enzymes. As indicated previously, the specification discloses the structure and function of the polypeptide of SEQ ID NO: 4 but it does not provide any information as to the structure and function of other enzymatic polypeptides having 70% sequence identity to SEQ ID NO: 4 or the bonds hydrolyzed by such enzymes. Furthermore, there is no disclosure of the critical structural elements an enzyme having 70% sequence identity to SEQ ID NO: 4 should have to hydrolyze the recited bonds (see

interpretation above, rejections under 35 USC 112, second paragraph) or to hydrolyze α-1,6 galactosyl bonds (i.e. α-galactosidase activity).

The state of the art teaches that determination of a polypeptide's function is unpredictable based on sequence homology. See the teachings of Bork (Genome Research, 10:348-400, 2000), Broun et al. (Science 282:1315-1317, 1998), Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) and Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) already discussed. Since the amino acid sequence determines the function of a polypeptide, one would require some knowledge and/or guidance as to how structure relates to function to isolate polypeptides with enzymatic activity which can hydrolyze any bond, including α-1,6 galactosyl bonds. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to hydrolyze any bond including α-1,6 galactosyl bonds, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate those polypeptides having enzymatic activity, as encompassed by the claim, and determine which bonds can be hydrolyzed by them, to practice the claimed method. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

16. Claim1-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants were advised in Paper No. 10, mailed on 5/14/2002 of a discrepancy between the sequence listing and CRF in regard to SEQ ID NO: 4. In response, Applicants have submitted a new paper and CRF sequence listing wherein the amended sequence listing presents a change in the first amino acid of SEQ ID NO: 4. Applicants have submitted that the first amino acid of SEQ ID NO: 4, which is a leucine, has been changed to methionine since those in the art would recognize that a start codon should encode a methionine.

Claims 1-12 are directed to a method for hydrolyzing bonds with the polypeptide of SEQ ID NO: 4. While Figure 1 as originally filed disclose a polypeptide of 364 amino acids wherein the first amino acid is a leucine, there is no support in the specification for the amended SEQ ID NO: 4, which now discloses a polypeptide of 364 amino acids wherein the first amino acid is a methionine. The specification discloses the polypeptide of SEQ ID NO: 4 as being a mature enzyme (page 3, last paragraph). As known in the art, mature polypeptides, in many cases do not retain an N-terminal methionine residue since they require modifications and/or processing such as the proteolytic cleavage of a signal peptide. Furthermore, it is known in the art that while most proteins have a methionine as their first amino acid, there are proteins which are not translated with methionine as the first amino acid. As such, one of skill in the art cannot reasonably assume that the first amino acid in a mature protein or a full protein is a methionine residue. In addition, there is no support in the specification for a polypeptide having 364 amino acids wherein the first amino acid residue is methionine. Since the polypeptide of SEQ ID NO: 4 as originally filed is not the same as that of the amended SEQ ID NO: 4, claims 1-12 are no longer directed to a method of use of the polypeptide of SEQ ID NO: 4 as originally filed but to a different polypeptide which has not been described. Thus, one of skill in the art cannot

reasonably conclude that Applicant was in possession of the claimed invention at the time the application was filed.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of U.S. Patent No. 5958751. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claim 2 of US Patent No. 5958751 is directed to a method for hydrolyzing bonds using a substantially purified enzyme having the amino acid sequence set forth in SEQ ID NO: 4. Since the polypeptide of SEQ ID NO: 4 in US Patent No. 5958751 appears to be the same as that of the instant application based on Figure 1 of such patent, the polypeptide of SEQ ID NO: 4 encodes an α-galactosidase. Claims 1-5 of the instant application are all directed to a method for hydrolyzing bonds using the polypeptide of SEQ ID NO: 4 or homologs having 70% sequence identity to the polypeptide of SEQ ID NO: 4. Therefore, claim 2 of US Patent No. 5958751 anticipates claims 1-5 of the instant application as written. Claims 6-9 of the instant application, drawn to the method of claim 1, add limitations in regard to the compound having the bond to be hydrolyze which do not render the claims patentably distinct since compounds which are hydrolyzed by α-galactosidases are well known in the art. Similarly, claims 10-12 of the instant application, drawn to the method of claim 1, add limitations in regard to pH and temperature which do not render the claims patentably distinct since the α-galactosidase of SEQ ID NO: 4 was isolated from an organism (T. alcaliphilus) which has optimal growth at the same pH and temperature recited in the claims, therefore there is a reasonable expectation that an enzyme from such organism should have optimal enzymatic activity at the same pH and temperature as those of optimal growth. Therefore, claims 6-12 of the instant applications would have been obvious over claim 2 of US Patent No. 5958751.

19. This rejection was applied to claims 1-9 in Paper No. 6, mailed on 9/28/2001 and is now applied to all pending claims (1-12) for the reasons discussed above.

20. Applicants have traverse the rejection but have not provided any arguments in response to the Examiner's contention. Furthermore, Applicants have requested that the rejection be held in abeyance until the claims are allowable.

21. Since no arguments have been presented and no terminal disclaimer has been filed, the double patenting rejection is maintained for the reasons of record.

22. Claims 1-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending application No. 10/114083. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claim 1 of copending application No. 10/114083 is directed to a method of catalyzing the hydrolysis of saccharides comprising contacting a saccharide with a polypeptide having the amino acid sequence of SEQ ID NO: 4 or homologs having at least 50% sequence homology to the polypeptide of SEQ ID NO: 4. Since the polypeptide of SEQ ID NO: 4 in copending application No. 10/114083 appears to be the same as that of the instant application based on Figure 1 of such application, the polypeptide of SEQ ID NO: 4 encodes an α-galactosidase. Claims 1-5 of the instant application are all directed to a method for hydrolyzing bonds using the

polypeptide of SEQ ID NO: 4 or homologs having 70% sequence identity to the polypeptide of SEQ ID NO: 4. Therefore, claim 1 of copending application No. 10/114083 anticipates claims 1-5 of the instant application, as written. Claims 6-9 of the instant application, drawn to the method of claim 1, add limitations in regard to the compound having the bond to be hydrolyze which do not render the claims patentably distinct since compounds which are hydrolyzed by α-galactosidases are well known in the art. Similarly, claims 10-12 of the instant application, drawn to the method of claim 1, add limitations in regard to pH and temperature which do not render the claims patentably distinct since the α-galactosidase of SEQ ID NO: 4 was isolated from an organism (T. alcaliphilus) which has optimal growth at the same pH and temperature recited in the claims, therefore there is a reasonable expectation that an enzyme from such organism should have optimal enzymatic activity at the same pH and temperature as those of optimal growth. Therefore, claims 6-12 of the instant applications would have been obvious over claim 1 of copending application No. 10/1140832.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

23. Applicant is advised that should claim 3 be found allowable, claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, since SEQ ID NO: 4 has 364 amino acids. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

24. No claim is in condition for allowance.

25. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

26. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
November 26, 2002

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1600
1600